

REMARKS

In the Final Action, Claims 1, 3, 5, 7-10, 12, 14-17, 19, 21-25, 27 and 29 are pending. Claim 1 has been rejected under 35 U.S.C. 102(b) as allegedly anticipated by Ford et al., (U.S. Patent No. 5,635,202) or Velraeds et al. (*App Env Microbio* 62(6): 1958-63, June 1996). Claims 1, 3, 5, 7, 10, 12, 14, 17, 19, 21-22, 25, 27 and 29 have been rejected under 35 U.S.C. § 102(b) as allegedly anticipated by U.S. Patent No. 5,645,830 to Reid et al. Claims 1, 3, 5, 7, 10, 12, 14, 17, 19, 21-22, 25, 27 and 29 have been rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Reid et al. (*Clin. Micro. Rev.* 335-44, 1990). Claims 1, 3, 5, 7, 10, 12, 14, 17, 19, 21-22, 25, 27 and 29 have been rejected under the judicially created doctrine of obviousness-type double patenting as allegedly over Claims 1-17 of U.S. Patent No. 6,479,051.

This Response addresses each of the Examiner's rejections. Applicants therefore respectfully submit that the present application is in condition for allowance or at least in better condition for appeal. Favorable consideration of all pending claims is therefore respectfully requested.

As a preliminary matter, Applicants observe that the present application contains 29 claims. Claims 4, 6, 11, 13, 18, 20, 26 and 28 have been cancelled, without prejudice. However, the Examiner states only Claims 1, 3, 5, 7-10, 12, 14-17, 19, 21-25, 27 and 29 are pending, without including Claim 2. Moreover, Claims 1, 3, 5, 7, 10, 12, 14, 17, 19, 21, 22, 25, 27 and 29 have been rejected, without indicating whether Claims 8-9, 15-16 and 23-24 are allowed.

Claim 1 has been rejected under 35 U.S.C. 102(b) as allegedly anticipated by U.S. Patent No. 5,635,202 to Ford et al., ("Ford et al.") or Velraeds et al. (*App Env Microbio* 62(6): 1958-63, June 1996). The Examiner alleges that both references teach application of

lactobacillus for the colonization of the urogenital tract to prevent and treat colonization of uropathogenic flora. The Examiner alleges both Ford et al. and Velraeds et al. teach oral administration of *lactobacillus*.

Applicants observe that Ford et al. merely teach a method of intra-vaginally administering *Lactobacillus* to treat vaginal yeast infections. Nowhere do Ford et al. disclose a method of orally administering one or more probiotic organisms, e.g., *lactobacillus*, to treat bacterial vaginal infections, as presently claimed in Claim 1. The oral administration route in Ford et al. is explicitly limited to treating diarrhea (see, e.g., Abstract of Ford et al.).

Velraeds et al. merely disclose an *in vitro* experiment which demonstrates that certain *lactobacillus* isolates can inhibit the initial adhesion of uropathogenic *Enterococcus faecalis* strain. Nowhere does Velraeds et al. disclose a method of orally administering one or more probiotic organism, e.g., *lactobacillus*, to treat bacterial vaginal infections, as presently claimed in Claim 1.

Nowhere does the prior art recognize that orally administered strains of bacteria can be used to make dairy products that colonize the vagina and thereby treat vaginal infections.

Thus, both Ford et al. and Velraeds et al. fail to teach each and every element of Claim 1, thereby do not sustain as a reference for a rejection under 35 U.S.C. § 102.

Therefore, the rejection of Claim 1 under 35 U.S.C. 102(b) is overcome and withdrawal thereof is respectfully requested.

Claims 1, 3, 5, 7, 10, 12, 14, 17, 19, 21-22, 25, 27 and 29 have been rejected under 35 U.S.C. § 102(b) as allegedly anticipated by U.S. Patent No. 5,645,830 to Reid et al. Specifically, the Examiner alleges that the '830 patent teaches oral administration of a probiotic.

Applicants observe that the '830 patent merely teaches a method for prevention of recurrent urogenital infection or post-antimicrobial infections by administering skim milk powder and/or one or more *Lactobacillus* strains to one suffering such infections. Nowhere does the '830 patent teach treating bacterial vaginal infections, let alone treating such infections via oral administration of probiotics, as disclosed and claimed by the present invention. Indeed, the present invention, for the first time, provides that oral intake of *Lactobacillus* can successfully deliver probiotic therapy to women in need thereof. Thus, Applicants respectfully submit that the present invention is not anticipated by the '830 patent.

Therefore, the rejection of Claims 1, 3, 5, 7, 10, 12, 14, 17, 19, 21-22, 25, 27 and 29 under 35 U.S.C. 102(b) is overcome and withdrawal thereof is respectfully requested.

Claims 1, 3, 5, 7, 10, 12, 14, 17, 19, 21-22, 25, 27 and 29 have been rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Reid et al. (*Clin. Micro. Rev.* 335-44, 1990). The Examiner is of the opinion that although Reid et al. do not teach oral administration of a probiotic in all the described specific experiments, Reid et al. somehow “discloses that *lactobacillus* was and can be administered orally.” However, the Examiner does not specifically indicate where that disclosure or suggestion is found in Reid et al. The Examiner merely cites page 339 and 340 of Reid et al. and alleges that Reid et al. teach the use of *lactobacillus* for treatment of urogenital infections.

In response, Applicants respectfully submit that Reid et al. fail to disclose that *lactobacillus* can be administered orally to treat vaginal infections, as recognized and claimed by the present invention. In fact, on the page cited by the Examiner (p. 339), Reid et al. clearly teach that *L. casei* GR-1 was implanted directly into the urinary bladder in postmenopausal

patients, i.e., *Lactobacillus* was administered intravesicularly. Thus, Applicants respectfully submit that Reid et al. do not anticipate the present invention.

Therefore, the rejection of Claims 1, 3, 5, 7, 10, 12, 14, 17, 19, 21-22, 25, 27 and 29 under 35 U.S.C. 102(b) is overcome and withdrawal thereof is respectfully requested.

Claims 1, 3, 5, 7, 10, 12, 14, 17, 19, 21-22, 25, 27 and 29 have been rejected under the judicially created doctrine of obviousness-type double patenting as allegedly over Claims 1-17 of U.S. Patent No. 6,479,051. The Examiner admits that Claims 1, 3, 5, 7, 10, 12, 14, 17, 19, 21-22, 25, 27 and 29 of the present invention and Claims 1-17 of the '051 patent are not identical. The Examiner acknowledges that the methods in the two inventions have different uses. However, the Examiner alleges that the methodologies used in the two cases are the same. Thus, the Examiner alleges that that claims of the present invention and those of the '051 patent are not patentably distinct from each other.

In the first instance, Applicants observe that Claims 10, 12 and 14 depend on Claim 8; Claims 17, 19, 21 depend on Claim 15; Claims 25, 27 and 29 depend on Claim 23. However, the Examiner does not reject Claims 8, 15 and 23. Nor does the Examiner reject Claims 9, 16, and 24, which depend on Claims 8, 15 and 23, respectively.

Applicants observe that Claims 1-17 of the '051 patent are directed to methods that establish a healthy urogenital flora while the present invention is directed to methods for treating bacterial vaginal infections (Claims 1, 3, 5, 7), treating vaginitis (Claims 8, 10, 12 and 14), reducing candida colonization, or treating bacterial vaginosis (Claim 23) and a pharmaceutical composition comprising specific *lactobacillus* strains.

Applicants respectfully submit that a rejection under the judicially created doctrine of obviousness-type double patenting requires that the alleged claims are obvious over


the patented claims. Applicants respectfully submit that a method that can treat bacterial vaginal infections or vaginitis, or reduce candida colonization is a different method from, and thereby patentably distinguishable from, a method that can establish a healthy urogenital flora.

Moreover, Applicants respectfully submit that the alleged claims of the present application not only have a different scope but also are not obvious over Claims 1-17 of the '051 patent. Applicants respectfully submit that the methods for treating bacterial vaginal infections or vaginitis, or reducing candida colonization are not obvious over the methods for improving vaginal health. For example, Baerheim et al. demonstrated (Baerheim et al., *Scand J Prim Health Care*. 1994 Dec;12 (4):239-43, a copy of the Abstract of Baerheim et al. is enclosed as Exhibit A) that just merely applying *lactobacilli* vaginally does not necessarily improve vaginal health. In fact, according to Baerheim et al., there is no difference at all. In another example, *lactobacilli* were present and the urogenital flora was healthy, but patients still suffered urinary tract infections (see Jackson et al. *Am J Med*. 2004 Dec 15;117(12): 903-11, a copy of the Abstract is enclosed as Exhibit B). Thus, Applicants respectfully submit that the claims of the present application are not obvious over and are clearly patentably distinct from the claims of the '051 patent.

Therefore, the rejection of Claims 1, 3, 5, 7, 10, 12, 14, 17, 19, 21-22, 25, 27 and 29 under the judicially created doctrine of obviousness-type double patenting over Claims 1-17 of U.S. Patent No. 6,479,051 is overcome. Withdrawal of the rejection is respectfully requested.

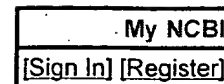
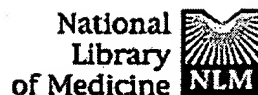
In view of the above, it is respectfully submitted that this application is in condition for allowance which action is earnestly solicited.

Respectfully submitted,


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☐ 1: Scand J Prim Health Care. 1994 Dec;12(4):239-43.

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Vaginal application of lactobacilli in the prophylaxis of recurrent lower urinary tract infection in women.

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OBJECTIVE--To examine whether vaginal application of *Lactobacillus casei* v. *rhannosus* reduces the reinfection rate in cystitis-prone women. **DESIGN**--A controlled, randomized, double-blind clinical trial. **SETTING**--Division for General Practice, University of Bergen, Norway. **INTERVENTION**--Vaginal application of lactobacilli twice weekly. **SUBJECTS**--47 women, aged 18-50 years, reporting three or more episodes of distal urinary symptoms during the previous 12 months, of which at least one episode had been medically verified as a lower UTI. **MAIN OUTCOME MEASURE**--The incidence rate of lower UTI during 6 months' follow-up. **RESULTS**--No difference in infection rate between the two groups; the incidence rate ratio between the treatment group and the placebo group was 1.41 (95% confidence interval 0.88-1.98). Lactobacilli were not found more frequently periurethrally in the treatment group than in the control group. **CONCLUSION**--It is still uncertain whether vaginal application of lactobacilli reduces the infection rate in cystitis-prone women.

Publication Types:

- Clinical Trial
- Randomized Controlled Trial

PMID: 7863140 [PubMed - indexed for MEDLINE]

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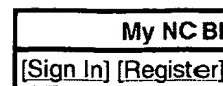
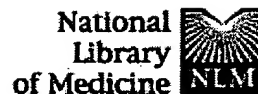
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☐ 1: Am J Med. 2004 Dec 15;117(12):903-11.

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Predictors of urinary tract infection after menopause: a prospective study.

Jackson SL, Boyko EJ, Scholes D, Abraham L, Gupta K, Fihn SD.

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PURPOSE: To describe the incidence of and risk factors for acute cystitis among nondiabetic and diabetic postmenopausal women. **METHODS:** We conducted a population-based, prospective cohort study of 1017 postmenopausal women, aged 55 to 75 years, who were enrolled in a health maintenance organization and followed for 2 years. A wide range of behavioral and physiologic exposures were assessed at baseline interview and follow-up clinic visits; the main outcome measure was microbiologically confirmed acute symptomatic cystitis. Follow-up was 87% at 12 months and 81% at 24 months. **RESULTS:** During 1773 person-years of follow-up, 138 symptomatic urinary tract infections occurred (incidence, 0.07 per person-year). Independent predictors of infection included insulin-treated diabetes (hazard ratio [HR] = 3.4; 95% confidence interval [CI]: 1.7 to 7.0) and a lifetime history of urinary tract infection (HR for six or more infections = 6.9; 95% CI: 3.5 to 13.6). Borderline associations included a history of vaginal estrogen cream use in the last month (HR = 1.8; 95% CI: 1.0 to 3.4), a history of kidney stones (HR = 1.9; 95% CI: 1.0 to 3.7), and asymptomatic bacteriuria at baseline (HR = 1.8; 95% CI: 0.9 to 3.5). Sexual activity, urinary incontinence, parity, postcoital urination, vaginal dryness, use of cranberry juice, vaginal bacterial flora, and postvoid residual bladder volume were not associated with incident acute cystitis after multivariable adjustment. **CONCLUSION:** Insulin-treated diabetes is a potentially modifiable risk factor for incident acute cystitis among postmenopausal women, whereas a lifetime history of urinary tract infection was the strongest predictor. Use of oral or vaginal estrogen was not protective, and a wide range of behavioral and physiologic factors was not associated with acute cystitis episodes in this generally healthy sample.

PMID: 15629728 [PubMed - indexed for MEDLINE]

Abstract Text